RECEIVED
OCT 13

Group VI: claims 1, 2, and 8-11;
Group VII: claim 12;
Group VIII: claim 13; and
Group IX: claims 14-18.

In view of the following remarks, Applicants respectfully request that the Examiner reconsider and withdraw the requirement for restriction among groups I through IX. Specifically, a requirement for restriction is proper if the inventions are independent and distinct as claimed, resulting in a serious burden to the Examiner if restriction were not required. Applicants respectfully submit that these requirements have been met.

The M.P.E.P. states that, "if the search and examination of an entire application can be made without serious burden, the examiner must examine [the application] on the merits, even though it includes claims to independent or distinct inventions." (M.P.E.P. 803, p. 800-3.) Applicants respectfully submit that, in view of the interrelatedness of the subject matter of claims 1-12, it would be no serious burden to the Examiner to search and examine the claims of Groups I-VII, all drawn to methods of treating or preventing renal disorders, together. Applicants further submit that examination of the claims of Groups I-IV together would save the Examiner time and effort, in view of the interrelatedness of the subject matter of these claims. For example, Groups I-IV each include claims 1, 2, and 9-11. Therefore, Applicants respectfully request reconsideration and withdrawal of the restriction requirement as to the claims in these groups.

Applicants further note that Groups II-VII are classified in the same class (514), and that Group IV-VII are classified in the same class and subclass (514, 866), demonstrating the lack of serious burden to the Examiner, and the economy of effort involved, if the restriction requirement is withdrawn as to these claims. Therefore, Applicants respectfully request reconsideration and withdrawal of the restriction requirement as to claims 1-12, the claims of Groups I-VII, and examination of these claims.

In addition, the Examiner states that the claims corresponding to Groups VIII and I-VII and IX recite subject matter related as product and process of use, but patentably distinct. (See

Restriction Requirement, page 3.) However, the Examiner provides no specific basis for a distinction between the subject matter recited in each of these claims. Furthermore, Applicants respectfully point out that the claims of Groups II-VIII share the same classification (Class 514). In addition, the claims of Groups III and VIII share the same subclassification (Class 514, subclass 43) and the claims of Groups IV-VII share the same subclassification (Class 514, subclass 866). Therefore, examination of these claims together would cause no serious burden to the Examiner.

Applicants also note that claim 13, the claim of Group VIII, is drawn to a pharmaceutical composition comprising an agent that modulates, regulates, or inhibits the activity of CTGF or fragments thereof. As this agent is the same agent recited in claims 1-12, no serious burden would result from examination of this claim together with claims 1-12. Therefore, Applicants further request reconsideration and withdrawal of the requirement for restriction and examination of claims 1-13.

Finally, Applicants further submit that a search of the art for methods of treating and preventing renal disorders (Groups I-VII) would necessarily reveal art directed to methods of diagnosing renal disorders (Group IX). Therefore, search and examination of these claims would result in no serious burden to the Examiner. Applicants thus respectfully request reconsideration and withdrawal of the restriction requirement as to the claims in these groups, and examination of the claims contained therein.

In summary, in view of the preceding remarks, Applicants request reconsideration and withdrawal of the restriction requirement at least as it applies to the claims of Groups I-IV, claims 1-6, 9, and 11. Applicants further request reconsideration and withdrawal of the restriction requirement among the claims of Groups I-IX. However, in order to comply with the provisions of 37 C.F.R. 1.143, Applicants hereby provisionally elect, with traverse, claims 14-18, the claims of Group IX. Applicants reserve without prejudice the right to pursue any non-elected subject matter in continuing applications.

II. Species Election

The Examiner further stated that "[i]rrespective of whichever Group applicant may elect, applicant is further required under 35 U.S.C. 121" to elect a method for treating, preventing, or diagnosing "a specific renal disorder such as diabetes or hypertension...." (Restriction Requirement, page 4.) The Examiner stated that "[t]hese disorders are distinct because the pathological conditions differ in etiologies and therapeutic endpoints." (*Id.*) Applicants respectfully disagree.

Chronic renal failure occurs in many etiologically diverse renal diseases, chronic or acute conditions often leading to irreversible scarring or damage, characterized as diffuse interstitial fibrosis. (Bohle et al. (1989) *Path. Res. Pract.* 185:421-440.) The onset and extent of renal fibrosis is highly correlated with increased expression and overproduction of CTGF. Further, CTGF expression is strongly up-regulated in a number of renal pathologies, indicating that CTGF is a common factor in the pathology of renal fibrosis associated with various conditions, such as, for example, diabetes, hypertension, hyperglycemia, glomerulosclerosis, and interstitial disease. (See, e.g., Hsueh and Anderson (1992) *Hypertension* 20:253-263; Riser et al. (2000) *J. Am. Soc. Nephrol.* 11:25-38; Ito et al. (1998) *Kidney International* 53:853-861; and Clarkson et al. (1999) *Curr. Opin. Nephrol. Hypertens.* 8:543-548.) The pathology of CTGF-induced overproduction and deposition of extracellular matrix within a diseased kidney occurs irrespective of the physiological condition leading to a particular renal disorder. Renal disorders in which kidneys display this pathology have common therapeutic endpoints, i.e., a decrease in excess levels of CTGF and the resultant decrease in excess production and deposition of extracellular matrix.

The present methods are directed to diagnosing a renal disorder or a predisposition to developing a renal disorder by detecting altered levels of CTGF expression and activity, and to preventing and treating such a renal disorder through modulation, regulation, or inhibition of the expression and activity of CTGF. Therefore, the renal disorders recited in the present methods are disorders characterized by altered levels of expression and activity of CTGF. These disorders, including, for example, diabetes and hypertension, are associated with increased production and deposition

of extracellular matrix material, and thus possess a common pathological condition. See, e.g., throughout the specification generally and in particular, for example, at page 3, lines 5-9, lines 17-20, and lines 26-30, and at page 4, lines 15-17. In addition, the recited renal disorders have common therapeutic endpoints, i.e., a decrease in excess levels of CTGF and a decrease in excess production and deposition of extracellular matrix.

Applicants further note that the claimed methods of diagnosis and treatment do not require identification of the etiology of every pathology characterized by a renal disorder associated with CTGF, and that such matter is not relevant to the patentability of the instant claims. For example, with respect to the present methods of diagnosing a renal disorder associated with altered expression or activity of CTGF, identifying the presence of a renal disorder associated with elevated levels of CTGF would be diagnostic of such a disorder, regardless of the etiology of that disorder.

In summary, the renal disorders recited in the instant claims are so closely related, in terms of pathology and therapeutic endpoint, etc., that a search and examination of each entire claim can be made without serious burden. (M.P.E.P. 803.02, p. 800-4.) For the above reasons, Applicants respectfully request reconsideration and withdrawal of the requirement for election of species.

In the event that the Examiner refuses to reconsider and withdraw the species election requirement, Applicants provisionally elect, with traverse, diabetes as the renal disorder in consideration of the instant claims. Claims 1-18 are readable thereon, as the present methods can be directed to the treatment, prevention, and diagnosis of diabetes, and the present pharmaceutical composition and diagnostic kit can be used in the course of such treatment, prevention, or diagnosis. Applicants note that the identification of diabetes as the disorder is made only for the purpose of complying with the instant election, and that Applicants reserve without prejudice the right to subsequently pursue the remaining subject matter. As noted by the Examiner, if the species requirement is upheld, Applicants will have opportunity to add claims relating to additional renal disorders upon allowance of the instant claims.

If there are any questions regarding the present communication or the above-referenced application, please call Applicants' Attorney at 650-866-7254.

Respectfully submitted,
FibroGen, Inc.

DATE: 5 October 00

Leanne C. Price, Esq.
Reg. No. 42,090

225 Gateway Boulevard
South San Francisco CA 94080
Main: 650-866-7200
Direct: 650-866-7254
Facsimile: 650-866-7204